EXHIBIT B

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: *Wave 4 Cases*	

Prolift General Report of Steven Goldwasser, M.D.

This report contains my general opinions regarding the design, safety, and efficacy of the Gynecare Prolift. It also contains a summary of my qualifications, training, education, and experience, which help form the basis of the opinions contained herein. The materials I have reviewed that support my opinions are either identified in this report or are set forth in my reliance list which will be provided with this report. All of the opinions in this report are held to a reasonable degree of medical certainty, and I reserve the ability to supplement or modify these opinions if additional information is received and/or reviewed.

BACKGROUND, TRAINING AND EXPERIENCE

I am board-certified in Obstetrics and Gynecology, with a subspecialty board certification in Female Pelvic Medicine and Reconstructive Surgery. I received my undergraduate education at the University of California, San Diego and my medical degree from Tulane University. I completed my residency in Obstetrics and Gynecology at the University of Tennessee, Memphis.

Subsequently, I completed a 2-year fellowship in Female Pelvic Medicine and Reconstructive Surgery at Good Samaritan Hospital in Cincinnati Ohio under the direction of Mickey Karram, MD. After completing my fellowship training in 2000, I joined the faculty at the University of Florida in Jacksonville where I started the division of Urogynecology. In 2006, I started my private practice in Jacksonville and I continue my association with the university as a clinical instructor.

I became a diplomate of the American Board of Obstetrics and Gynecology in 2002 and became subspecialty certified in Female Pelvic Medicine and Reconstructive Surgery (FPMRS) in 2013. I have had a Florida Medical License continuously for the past 16 years. My hospital affiliations include Baptist Medical Center, St. Vincent's Medical Center, and the University of Florida Medical Center, Jacksonville.

During the course of my career, I have received extensive training in female pelvic medicine and reconstructive surgery, including vaginal, abdominal, laparoscopic, robotic, and non-surgical approaches for treating pelvic organ prolapse and urinary incontinence. I have obtained extensive experience in both the design and implementation of various prolapse repair techniques involving native tissue repair and augmentation procedures using both biologic and synthetic graft materials. During my residency, the focus of reconstructive surgery was centered on native tissue repair. During my fellowship, we began incorporating biologic tissues into reconstructive surgery for prolapse repair and transitioned from biologic slings to the original retropubic TVT procedure (1998). Early in my career at the University of Florida in 2000, I continued to use biological graft augmentation for vaginal prolapse repairs and gradually introduced free cut Gynemesh PS. With the introduction of the Posterior IVS Tunneller in 2001, I became a consultant with US Surgical and started a course towards research and development with extensive cadaver dissection work.

I began using the Prolift system in 2005 and continued to use the system until it was voluntarily removed from the market in 2012. During that time period, I implanted approximately 300 Prolift devices, and also served as an instructor for Ethicon. As an instructor, I trained numerous physicians with both didactic and cadaveric teaching sessions. In addition to the hands-on training and other written materials, Ethicon provided physicians with amazing 3-D renderings of pelvic anatomy incorporating the Prolift system. I still use these instructional tools to help residents, fellow physicians and even patients better conceptualize the intricacies of anatomy and incorporation of pelvic reconstructive surgery techniques.

My extensive clinical training and cadaver dissection experience led to my development and implementation of several devices and techniques for reconstructive pelvic surgery. During the course of product development and as an instructor for physician training, I dedicated considerable time to cadaver lab dissection. This experience led to a collaborative effort with my urology colleague from the University of Florida. Ultimately we developed the EXAIR, a novel polypropylene mesh graft-based approach for treating vaginal prolapse.

Additionally, in the process of both research and clinical practice, we started a vaginal prolapse database. Our data collection started with our first Prolift procedure in 2005 and continues to the present (over 450 patients to date). This is an ongoing mesh-based prolapse repair database of our surgical experience and patient outcomes. From this database, we have produced several abstracts and clinical presentations. Furthermore, I continue to use the ongoing information to guide my patient counseling and surgical approach for vaginal prolapse.

In total, I have performed well over 1000 surgical procedures to treat pelvic organ prolapse, and used synthetic mesh augmentation from various manufacturers in over 500 procedures. I have also performed over 1000 surgical procedures to treat stress urinary incontinence, and used polypropylene mesh in the majority of those procedures. Given my

background, training, education, and experience, attendance and participation in medical meetings, and teaching other physicians, I am familiar with, and can testify regarding, the relative risks and benefits of the various approaches for treating pelvic organ prolapse, as well as the possible complications for the various approaches. In addition, a portion of my practice involves re-operative management of recurrent prolapse and urinary incontinence, as well as treating and managing complications associated with native tissue repairs, transvaginal mesh, and sacralcolpopexies. I also have considerable experience treating complex female pelvic pain, sexual dysfunction, complex urinary incontinence, recurrent urinary tract infections, and other pelvic complaints in patients. Therefore, I understand, and can testify about, contributing causes of different patient complaints, as well as the best ways to avoid, minimize, or treat complaints when they occur.

I am also familiar with, and can testify regarding, the development and application of polypropylene based mesh materials incorporated in repairing vaginal prolapse and female stress urinary incontinence, as well as the appropriate surgical applications for transvaginal mesh and the associated risks and benefits. I am also aware of and can testify regarding how physicians are trained, what information is provided during their training, how physicians get information they rely on in performing surgical procedures, and the different ways physicians remain knowledgeable of the data and advances in medicine relevant to this field.

A copy of my CV, which further details my training, education and experience, is attached to this report.

PROLAPSE BACKGROUND

Pelvic organ prolapse represents a female hernia. It is the descent of female pelvic organs such as the uterus (uterine prolapse), urethra (urethrocele), bladder (cystocele) and rectum (rectocele) into the vaginal canal and in some cases beyond the introitus. In the case of the post

hysterectomy patient, this may involve the small intestine (enterocele) as well. These structures are normally held into position via interaction between the boney pelvis, the pelvic floor muscles and extensive connective tissue. Dmochowski RR, Gomelsky A. 26 Cystocele and Anterior Vaginal Prolapse. In Graham SD, Glenn JF, Keane TE eds. Glenn's Urologic Surgery, 6th edn. Philadelphia, PA: Lippincott Williams & Wilkins, 2004: 339–48 27. The boney pelvis functions an anchoring point for the fascial covering of the pelvic floor muscles, which in turn supports the pelvic contents. The pelvic muscles consist of the obturator internus (along the lateral pelvic sidewall) and the bowl-shaped levator ani, which joins the obturator internus at the arcus tendineus fasciae pelvis ("ATFP"). The pelvic organs ("PO") of the anterior compartment are surrounded by the endopelvic fascia, which anchors the POs to the musculature and the musculature to the bony pelvis. The vaginal aspect of this fascia is referred to as the pubocervical fascia. A defect in the pubocervical fascia results in a central cystocele. Central defects are often associated with loss of Level I support at the cardinal ligaments and may present with a concomitant enterocele. The lateral condensation of these fasciae is called the arcus tendineous fascia pelvis, also known as the White Line. The White Line serves as the anchoring point to the pelvic sidewall. A break in the lateral attachment results in a displacement cystocele. Defects of bladder support may be central, lateral, or a combination of both.

When evaluating vaginal support cephalad to caudad, the cardinal ligaments anchor the upper vagina and cervix to the pelvic sidewall (Level I support). In the mid-vagina, the pubocervical fascia extends from the White Line to support the bladder base and the anterior vaginal wall (Level II support). The posterior vaginal wall is attached laterally to the fascia overlying the levator ani muscle. In the anterior vagina, Level III support is considered to originate from the urethropelvic ligaments providing support to the urethra.

In the posterior compartment, the vagina is separated from the rectum by the rectovaginal septum. Both the pubocervical fascia in the anterior compartment and the rectovaginal septum are trapezoidal, with the narrow end located distally. The rectovaginal septum is fused proximally with the urogenital diaphragm and distally to the perineal body (Level III support) and is attached laterally to the arcus tendineus fasciae rectovaginalis in the distal one-third of the vagina and to the ATFP in the proximal two-thirds. Proximally, the septum fuses with the uterosacral ligaments laterally and the pericervical ring centrally.

As in the anterior compartment, posterior compartment defects in the rectovaginal septum may be central or lateral. Likewise, proximal detachment of the rectovaginal septum from the uterosacral ligaments may be associated with an enterocele, while disruption of the distal attachment to the perineal body may result in downward descent of the perineal (perineocele). Re-approximation of the perineal body (perineorrhaphy) addresses a weakness in the perineum, while a plication of the rectovaginal fascia in the midline (posterior colporrhaphy) has been traditionally used to repair a central posterior compartment defect. Additionally, a 'site-specific' posterior repair has been described that addresses discrete tears in the rectovaginal fascia in lieu of a midline plication. Additionally, procedures for concomitant apical prolapse (suspension from the sacral promontory, uterosacral, sacrospinous or iliococcygeus) may be necessary to repair concomitant apical compartment defects.

ETIOLOGY

Pelvic organ prolapse is a highly prevalent condition affecting about 50% of parous women. Maher C, et al., Surgical management of pelvic organ prolapse in women. Cochrane Database of Systemic Reviews 2013. There is a lifetime risk of approximately 12% that a woman in the United States will undergo a surgical procedure to treat pelvic organ prolapse. Wu J, et al., Lifetime Risk of Stress Urinary Incontinence or Pelvic Organ Prolapse Surgery. Obstet

Gynecol 2014;123: 1201-6; also Olsen AL, et al., Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol 1997 Apr;89(4):501–506; Fialkow MF, et al., Lifetime risk of surgical management for pelvic organ prolapse or urinary incontinence. Int Urgogynecol J Pelvic Floor Dysfunct 2008 Mar;19(3):437–440. Some have estimated the annual cost in the United States of pelvic organ prolapse is more than one billion dollars, with more than 300,000 pelvic floor surgeries. Subak LL, et al., Cost of pelvic organ prolapse surgery in the United States. Obstet Gynecol 2001 Oct;98(4):646–651.

The development of pelvic organ prolapse is multifactorial as it relates to damage or weakening of the supporting structures in the pelvis. Some of the more common factors thought to be associated with prolapse are events that cause a sudden or chronic rise in intra-abdominal pressure, for example, heavy lifting, chronic constipation, chronic cough. Olsen AL, et al., Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol 1997 Apr;89(4):501–506. Other factors that may contribute include: age, parity smoking, obesity, vaginal delivery, menopausal state, connective tissue disorders, pelvic trauma and prior pelvic surgery. Additionally, a patient's body structure can play a role as a large genital hiatus has been noted as being associated with vaginal prolapse. Lowder, Jerry L, et al., Genital hiatus size is associated with and predictive of apical vaginal support loss. American Journal of Obstetrics & Gynecology, Volume 214, Issue 6, 718.e1 - 718.e8.

PROLAPSE SYMPTOMS AND QUALITY OF LIFE

Prolapse symptoms and their associated physical findings vary tremendously. Most women will develop some degree of vaginal prolapse over their lifetime; however, not all of those women will become symptomatic. It is oftentimes difficult to make a clear association between subjective symptoms and objective physical findings. Some of the generalized common symptoms associated with vaginal prolapse include the sensation of something falling out of the

vagina, a palpable vaginal bulge, vaginal pressure, vaginal irritation, recurrent urinary tract infections ("UTIs") and low back pain. Some women may also associate prolapse with dyspareunia, pelvic pain, overactive bladder, urinary incontinence, obstructed voiding, constipation and obstructed defecation. Sometimes women will deny any of the above symptoms; however, they are bothered by the physical presence of their prolapse as it affects their body image and/or they have a concern that something "just is not right."

Many of the above symptoms are multifactorial and are niknot always directly linked with vaginal prolapse. For those who are symptomatic, prolapse can have a tremendous negative impact on quality of life, including, among many other things, social isolation, withdrawal from activities, and decreased sexual intimacy.

DIAGNOSING PROLAPSE

Determining the type or types of vaginal prolapse can be extremely challenging and highly variable. Prolapse is best demonstrated during a time of increased abdominal pressure (cough or Valsalva). Other factors affecting the examination include patient positioning, cooperation, time of day and level of physical activity (typically more pronounced at the end of the day and after physical activity). The patient is often examined in both supine and standing with an empty bladder. The patient is asked to generate a cough and/or Valsalva. At this point the physician attempts to determine the location(s) of the anatomical defect(s). During the examination, the physician is evaluating the anterior, posterior and apical segments of the vagina. Defects may be isolated but typically include aspects of various segments to some degree. This subjective evaluation is then objectively graded with either the POPQ or the Baden-Walker grading system.

TREATMENT OPTIONS

Treatment options for vaginal prolapse range from watchful waiting, physical therapy, mechanical reduction with a supportive pessary, to surgical intervention. The decision process on how to manage prolapse is very complex. Many factors must be taken into account including symptoms, the degree and type or types of prolapse, in addition to patient expectations, age, degree of physical activity, sexual function, physical health, medical co-morbidities, reproductive status and body habitus.

For patients with very mild to boarder-line symptoms and a lesser degree of prolapse, simple lifestyle changes in exercise, diet and initiating pelvic floor exercises may be effective.

The next level of intervention may include a vaginal pessary. A pessary is a reusable removable device that is inserted into the vagina to provide support. A variety of different size and shape pessaries are available. Some pessaries are designed to reduce vaginal prolapse and/or treat stress urinary incontinence. Depending upon the type of prolapse, size of prolapse, genitle hiatus and patient dexterity a pessary may or may not be appropriate. Eighty-five percent of women who attempt pessary use are able to use one successfully. Lamers BH, et al., Pessary treatment for pelvic organ prolapse and health-related quality of life: a review. Int Urogynecol J. 2011 Jun;22(6):637-44. However, many women who are excellent candidates for a pessary would rather "fix the problem" with a surgical approach or they may find pessary use to be inconvenient or uncomfortable. In addition, patients are required to periodically remove pessaries and their use can be associated with, among other things, discharge, odor, and vaginal erosions. Aries BE, Ridgeway B, et al., Int Urogynecol J 2008;19:1173-78.

Depending upon the multiple factors as mentioned above, two surgical options may be available: (1) reconstructive and (2) obliterative. There are also two surgical approaches that can be employed: (1) transvaginal approach for reconstructive or obliterative procedures; or (2) abdominal approach for either open, laproscopic or robotic procedures. Once the anatomical

approach is established there are a variety of individual procedures and combination of procedures – each with a tremendous amount of variability that accounts for the lack of standardization.

Additionally each technique may incorporate the following: (1) Native tissue repair with permanent or absorbable sutures (or a combination); (2) Tissue augmentation – Biological grafts (human or animal); or (3) Mesh grafts (permanent vs absorbable materials or a combination of the two).

The surgical option for treating vaginal prolapse is extremely challenging as the natural support complex and why it fails is multifactorial and not clearly understood. The traditional approach involving native tissue plication and suspension has a very high failure rate. Recurrent pelvic organ prolapse after surgical correction is one of the most vexing problems in reconstructive pelvic surgery. For example, approximately 30% of prolapse and urinary incontinence surgery that was performed in one community-based sample in the United States was for recurrent problems. Olsen AL, et al., Epidemiology of surgically managed pelvic organ prolapse and urinary incontinence. Obstet Gynecol 1997;89:501-06. Yet, reoperation is not synonymous with recurrence, because many women do not seek repair of recurrent prolapse; thus, the prevalence of prolapse recurrence (depending on the definition) may be even higher. Whiteside James L, et al., Risk factors for prolapse recurrence after vaginal repair, American Journal of Obstetrics and Gynecology (2004) 191, 1533-8.

NATIVE TISSUE REPAIR

ANTERIOR REPAIR:

The native tissue colporrhaphy dates back to Dr. Howard Kelly at The Johns Hopkins Hospital in the early 20th century. A native tissue repair involves a split thickness dissection of the vaginal wall. This dissection results in a layer of tissue referred to as “fascia” however it is

not true fascia. The tissue dissection is extremely variable depending on physician technique and the thickness of the vaginal mucosa.

There is controversy regarding the amount of supportive tissue or fascia in the anterior vaginal wall. Although the wall is composed of mucosa, muscularis, and adventitia and abuts a similar arrangement in both the urethra and bladder, various authors have attributed to it a vaginal fascial layer. Weber AM, Walters MD, Anterior vaginal prolapse: review of anatomy and techniques of surgical repair. Obstet Gynecol. 1997;89:311–318. Weber and Walters cited many articles on both sides of the controversy and reported no specific fascial layer, whereas DeLancey demonstrated a fascial layer suburethrally on the anterior vaginal wall. DeLancey JO, Structural support of the urethra as it relates to stress urinary incontinence: the hammock hypothesis. Am J Obstet Gynecol. 1994;170:1713–1723.

The Anterior repair (colporrhaphy) involves plication of the vaginal fascia under the bladder to support a central defect. This can be performed in multiple layers depending on the tissue dissection. The surgeon may use interrupted delayed absorbable or permanent sutures in a mattress fashion. Excess vaginal mucosa is trimmed and the resulting vaginal mucosa is closed. A paravaginal defect repair may also be performed if the surgeon thinks there is a lateral detachment from the pelvic sidewall. This type of repair can be approached transvaginally or abdominally. The paravaginal space is entered and an attempt is made to identify the arcus tendineus (endopelvic fascia / white line) that spans from the pubis to the ischial spine on both sides of the pelvis. Next, the anterolateral vaginal sulcus and fascia under the bladder is sutured to the white line to close the paravaginal defect(s).

The anterior repair can also be performed with graft augmentation. Because it is very difficult to identify the various specific site defects, a graft can be introduced to address both central and paravaginal support failure. Given the extreme anatomic variability, it is a challenge

to find adequate, reproducible supportive structures for attaching the graft. Graft fixation was initially performed by suturing the material (biologic or synthetic) to the pelvic sidewall. The surgeon attempts to identify a subjectively "good" supportive area to suture the graft to the sidewall while avoiding injury to the ureter, surrounding organs and the variable neurovascular complex.

POSTERIOR REPAIR:

The posterior repair (colporrhaphy) is performed in a similar fashion as the anterior repair. This repair is performed most often via the transvaginal approach. The posterior vaginal wall is incised and the underlying tissue with or without the levator ani muscles are plicated with either interrupted delayed absorbable or permanent sutures in a mattress fashion. The excess vaginal mucosa may be excised and the remaining mucosa is reapproximated with absorbable suture. Alternatively, some surgeons believe in a site specific approach. This technique generally avoids levator muscle midline plication and instead an attempt is made to identify specific fascial breaks and close them with suture (again delayed absorbable or permanent sutures in a mattress fashion).

APICAL VAGINAL PROLAPSE / UTERINE PROLAPSE REPAIR:

There are 2 anatomical approaches for the apical defect repair: the transvaginal and the abdominal approach. The most common transvaginal procedures include the sacrospinous ligament fixation (SSLF), modified McCall culdoplasty, iliococcygeus suspension, and high uterosacral ligament suspension. These procedures all incorporate either permanent or delayed absorbable suture material. These procedures may also incorporate a vaginal hysterectomy.

The most common abdominal procedure for apical prolapse is the abdominal sacrocolpopexy (ASC). It can be performed through a laparotomy incision, laproscopically, and

robotically. It is often considered the "gold standard" for vault repair. In this procedure, a permanent or biologic mesh graft is attached to the vaginal apex, anterior and posterior vaginal walls. The graft is then retroperitonalized and attached to the anterior longitudinal ligament over the sacral promontory. It has been shown to restore normal pelvic anatomy and function better than vaginal repair and its results are longer lasting. Maher C, et al., Surgical management of pelvic organ prolapse in women. Cochrane Database of Systemic Reviews 2013. While abdominal surgery may be more durable, it is also more invasive and is associated with longer operative times, longer recovery times, and higher costs. It is most likely that the use of mesh, and not the abdominal route employed, gives this procedure its durability. The abdominal sacrocolpopexy also carries certain risks, such as small bowel injury, sacral osteomyelitis, and major hemorrhage due to injuring the middle sacral artery, which are not present in vaginal repairs. Thus, the benefits of the procedure must be balanced against other factors. Maher C, et al., Surgical management of pelvic organ prolapse in women. Cochrane Database of Systemic Reviews 2013.

NATIVE TISSUE REPAIR SURGICAL RESULTS

Transvaginal native tissue repairs for reconstructive surgery, in general, have the highest failure rates (50-60% in certain studies). Altman D, et al., Nordic Transvaginal Mesh Group (2011), Anterior colporrhaphy versus transvaginal mesh for pelvic-organ prolapse. N. Engl. J. Med. 2011 364(19):1826-1836; Hardiman PJ, Drutz HP, Sacrospinous vault suspension and abdominal colposacropexy: success rates and complications. Am J Obstet Gynecol 1996; 175:612-6; Benson JT, et al., Vaginal versus abdominal reconstructive surgery for the treatment of pelvic support defects: a prospective randomized study with long-term outcome evaluation. Am J Obstet Gynecol 1996; 175:1418-22; Whiteside JL, et al., Risk factors for prolapse recurrence after vaginal repair, American Journal of Obstetrics and Gynecology (2004) 191,

1533-8.; Maher C, et al., Surgical management of pelvic organ prolapse in women. Neurourol Urodynam 2008;37:3-12.

The anterior vaginal wall overall is the compartment most subject to surgical failure. This is possibly due to greater exposure to intra-abdominal strain and greater dependence on intact supportive structures. Maher, et al. reported that traditional anterior repair was associated with more anterior compartment prolapse on examination than for any polypropylene (permanent) mesh repair. Maher C, et al., Surgical management of pelvic organ prolapse in women. Cochrane Database of Systemic Reviews 2013. Awareness of prolapse was also higher after the anterior native tissue repair as compared to polypropylene mesh repair (28% versus 18%, RR 1.57, 95% CI 1.18 to 2.07).

Native tissue repairs have better but still poor anatomic results in the posterior compartment (failure rate of 25% or less). Culligan PJ, Surgical Repair of the Posterior Compartment. Clinical Obstetrics and Gynecology, Vol. 48, No. 3, 704-712 (2005). In general, native tissue repairs often fail due to absorption of the sutures or because permanent sutures may break or pull through weakened tissue which leads to recurrent prolapse. Reoccurrence is a significant issue, as women will often not pursue further surgery and will have to learn how to live with pelvic organ prolapse. Native tissue repair follow-up greater than 5 years is lacking, and many experts would agree that success rates of native tissue repair would most likely be even lower if the patients were evaluated for longer time periods.

GRAFT AUGMENTED REPAIRS

Augmenting colporrhaphy-based repairs with graft material developed due to the poor outcomes associated with native tissue colporrhaphy procedures. Augmenting repairs with graft material attempts to replace the weakened native tissue with a more durable material, which was being done successfully in abdominal and inguinal hernia repair procedures. Different biological

grafts have been used in colporrhaphy repairs, but these materials have been shown to be lees durable than polypropylene mesh graft augmentation. Maher CM, Baessler K, et al., 5th ICI. Paris: Health Publications, Ltd; 2013.

EVOLUTION OF MESH

Surgical mesh was designed in the 1950s to correct abdominal wall hernias. The woven material is placed below the skin to patch the weakened area in the abdomen and block intestines and other tissues from protruding. Abdominal wall hernia repair with mesh is now standard in most countries and widely accepted as superior to primary suture repair. As a result, there has been a rapid growth in the variety of meshes available. In 1958, Usher published his technique using a polypropylene mesh. This led to the Lichtenstein repair years later, which popularized mesh for hernia repair. In 2002, the EU trial collaboration analyzed 58 randomized controlled trials and found that the use of mesh was superior to other techniques. The EU Hernia Trialists Collaboration. Repair of groin hernia with synthetic mesh: meta-analysis of RCT. Ann Surg. 2002;235:322–32. They observed fewer recurrences and less postoperative pain with the mesh repair. Mesh has now virtually replaced suture repair of abdominal wall hernia in the developed world.

The successful treatment of hernias with surgical mesh led doctors to consider using it in other parts of the body that required additional support. In the 1950s gynecologists first recognized the need for graft augmentation in prolapse surgery to improve the disappointing surgical outcomes from vaginal colporrhaphy. Around 1962, the abdominal sacrocolpopexy (ASC) began to be performed. Lane first described the use of graft material for sacrocolpopexy procedures (e.g., harvested fascia lata, abdominal fascia, cadaveric fascia lata, Marlex, Prolene, Gore-Tex, Mersilene) with variable success rates. Lane F.E., Repair of posthysterectomy vaginal-vault prolapse. Obstet Gynecol 20: 72–77.

In 1970, Morgan reported the use of Marlex for stress urinary incontinence (SUI). In 1998, the Ethicon retropubic TVT sling device was introduced in the United States – it is composed of a Type 1 macroporous, monofilament polypropylene mesh. The TVT quickly became the gold standard for treating female SUI.

In 2002, Gynemesh PS (soft polypropylene) mesh was introduced for prolapse surgery. It is also a lightweight Type 1 macroporous, monofilament polypropylene mesh with a pore size of 2.4mm and a light weight of 42 g/m^2. It continues to be used as a bridging material for apical vaginal and uterine prolapse where surgical treatment (laparotomy or laparoscopic approach) is warranted. In 2005, the Prolift system became available. The unique system includes a precut Gynemesh PS graft and incorporates specialized instrumentation that facilitates graft placement and anchoring. The Prolift system uses boney landmarks to facilitate a much more standardized approach to transvaginal prolapse repair.

Several years later, Ethicon introduced another mesh product, which has an absorbable and non-absorbable component (Prolift+M). While this mesh was designed to be slightly heavier at the time of implantation (57 g/m^2 vs. 43 g/m^2), after absorption, the Prolift+M mesh has a lighter weight (28 g/m^2) and somewhat larger pore size (4.0 mm vs. 2.4 mm). However, the data and my personal experience have not shown a significant difference in exposure rates or dyspareunia rates between the two meshes. Overall clinical data on the compatibility of both Gynemesh PS and the mesh used in Prolift+M show that both meshes are effective and suitable for use in repair of pelvic organ prolapse.

All of the Ethicon mesh products noted above are classified as Type 1 mesh under the Amid mesh classification first published in 1997. The Amid classification separates materials based on pore size, which can impact infectious risk and tissue integration. In general, a pore size of >75 µm is considered macroporous and is desirable, as it allows passage of leukocytes

and macrophages. This is classified as a Type 1 Mesh. Woven meshes and meshes with smaller pore sizes (< 75 µm) allow bacteria to pass into the material and evade the host's defense mechanisms (leukocytes and macrophages cannot pass into the material). Additionally, pore size of >75 µm (Type 1 Mesh) also allows capillary and tissue growth into the mesh pores, which prevents encapsulation and promotes support to the prolapsed organ(s). The pore size of Gynemesh PS, which is used in Prolift, is approximately 2.5 mm or 2,500 µm, which easily accommodates the cells and small blood vessels needed to access the pores, promotes tissue integration, and reduces the risk of infection.

Some argue that polypropylene mesh grafts for prolapse surgery should have an even greater pore size and be even lighter in weight. However, use of Ultrapro in the Prolift+M resulted in mesh exposures and dyspareunia occurring at comparable rates. A larger pore lighter weight mesh—Vypro—was tried by the TVM Group, but it had many complications and was found not suitable for use in the pelvic floor. Denis S, et al., Pelvic Organ Prolapse Treatment by the Vaginal Route Using a Vypro Composite Mesh: Preliminary Results About 106 Cases. ICS IUGA 2004;(Abs. 620).

Type 1 mesh remains the preferred material for vaginal reconstructive surgery. It has numerous advantages over other graft materials including a low failure rate in incontinence and prolapse surgery. Mesh grafts are especially useful in certain patients, including those with recurrent pelvic organ prolapse or who are at higher risk of having recurrent pelvic organ prolapse. Despite its advantages, there are well-known complications, which must also be considered (discussed below). Virtually all of the complications associated with mesh repairs are also known to occur with native tissue and biological tissue augmentation repair as well.

THE PROLIFT SYSTEM

The Prolift system was designed by a group of surgeons over several years. Berrocal J, et al., Conceptual advances in the surgical management of genital prolapse. J Gynecol Obstet Biol Reprod 2004;33:577–587. The goal was to overcome the lack of standardization and poor anatomical and clinical success rates with current transvaginal procedures. The Prolift kit is a pre-cut piece of Type 1 soft Prolene polypropylene mesh and curved trocars with overlying guides used to insert the mesh graft. This specialized instrumentation facilitates fixation to pelvic structures that are otherwise very difficult to access. The trocars are passed under digital guidance (using fixed boney landmarks) to fixation points in the obturator membrane and the sacrospinous ligaments. The surgeons considered a number of different meshes, and Gynemsh PS was selected because of its design characteristics.

Prior to the development of Prolift, reconstructive pelvic surgery had been impossible to standardize. Variability includes the surgical dissection, patient anatomy, surgical exposure and tissue quality. The surgical dissection varies between physicians as does the patients anatomy, exposure and subjective tissue quality from patient to patient. The Prolift system was a huge leap forward in reproducibility and standardization in terms of technique. This system used fixed boney landmarks to better standardize the surgical approach, graft deployment, and fixation. Despite the advances in standardization, patient soft tissue anatomy continued to be the variable that ultimately can result in inconsistent surgical dissection that subsequently can affect patient outcomes using the Prolift system.

PROLIFT CLINICAL DATA

As discussed above, prior to the Prolift system becoming commercially available to the United States in 2005, it was developed and extensively studied by a group of French surgeons (TVM Group). These physicians organized a very large clinical trial to evaluate the safety and efficacy of the Prolift procedure. The study included over 300 patients treated since 2002. The

study was ongoing and grew to 687 patients when Cosson, et al. reported on it in 2005. Cosson M, et al., Prolift (Mesh (Gynecare) for Pelvic Organ Prolapse Surgical Treatment Using the TVM Group Technique: A Retrospective Study of 687 Patients. ICS 2005; Abs. 121. The scale of this study was revolutionary for prolapse-related mesh products and well beyond any pelvic organ prolapse industry standard. The study demonstrated that Prolift is safe and effective with a high success rate and minimal complications. The success rate was 89%, exposure rate was 13.3%, with dyspareunia almost non-existent. These results have further been confirmed with multiple post-launch clinical, long-term studies, and my own clinical practice.

The TVM Group also evaluated Vypro mesh, a larger-pore multifilament mesh composed of half of absorbable (polyglactin 910) and half of non-absorbable (polypropylene) fibers and determined that it was not suitable for use in pelvic floor reconstruction. Denis S, et al., Pelvic Organ Prolapse Treatment by the Vaginal Route Using a Vypro Composite Mesh: Preliminary Results About 106 Cases. ICS IUGA 2004;(Abs. 620).

Notably, the Prolift system and Gynemesh have been extensively studied – more so than any other mesh product for treating pelvic organ prolapse. In general, the data shows a clear benefit over native tissue repairs. Benefits include better procedural standardization, more durable anatomical and symptomatic improvement, and dyspareunia at a rate equivalent and in many cases better than native tissue repairs. The main procedure-related complication is mesh exposure. In my experience, both subjectively and also based on the objective multi-year data from my personal database, mesh exposure is likely due to a combination of surgical dissection and subjective patient tissue quality. Both of these factors are highly variable on a case-by-case basis. My opinion has been echoed in several studies. Jambusaria, et al. noted that the increased risk of complication related to vaginal mesh exposure may be related to the surgical technique, specifically the depth of dissection of the vaginal wall. Jambusaria LH, Murphy M, Lucente VR.

One-year functional and anatomic outcomes of robotic sacrocolpopexy versus vaginal extraperitoneal colpopexy with mesh. Female Pelvic Med Reconstr Surg 2015;21:87–92. Marschke, et al. and Murphy, et al. also reported the surgical technique and experience are key factors for a low erosion rate (3.2%) and complications. Marschke J, Hengst L, Schwertner-Tiepelmann N, Beilecke K, Tunn R. Transvaginal single-incision mesh reconstruction for recurrent or advanced anterior vaginal wall prolapse. Arch Gynecol Obstet 2015;291:1081–1087; Murphy M, Holzberg A, van Raalte H, Kohli N, Goldman HB, Lucente V, et al., Time to rethink: an evidence-based response from pelvic surgeons to the FDA Safety Communication. Update on serious complications associated with transvaginal placement of surgical mesh for pelvic organ prolapse. Int Urogynecol J 2012;23:5–9.

The use of vaginal mesh augmentation has now been shown in multiple RCTs and in large meta-analysis to decrease the risk of prolapse recurrence, especially anterior prolapse.

For example, Jacquetin published a table showing a number of randomized controlled trials in which transvaginal synthetic mesh or mesh kits were superior to traditional native tissue repair procedures for the treatment of pelvic organ prolapse. Jacquetin B, et al., Total transvaginal mesh (TVM) technique for treatment of pelvic organ prolapse: a 5-year prospective follow-up study. Int Urogynecol J 2013 Oct;24(10):1679–1686.

Int Urogynecol J

Table 1 Randomised controlled trials comparing polypropylene mesh with traditional native vaginal tissue repairs

Reference	Total number patients	Follow up (months)	Compartment studied	Anatomic cure mesh (%)	Anatomic cure traditional (%)	p
Hiltunen et al. [9]	104	12	Anterior	93	62	<0.04
Sivaslioglu et al. [10]	90	12	Anterior	91	72	<0.05
Nieminen et al. [11]	105	24	Anterior	89	59	<0.05
Nguyen and Burchette [12]	75	12	Anterior	87	55	<0.05
Carey et al. [13]	139	12	Anterior Posterior	81	65.6	0.07
Nieminen et al. [14]	202	36	Anterior	87	59	<0.0001
Withagen et al. [15]	194	12	All	90	55	<0.001
Altman et al. [16]	389	12	Anterior	82	48	0.008
Sokol et al. [17]	65	12	All	38	30	0.45

De Landsheere reported on a single center retrospective trial of 524 patients with a median follow-up of 3 years. de Landsheere L, et al., Surgical intervention after transvaginal Prolift mesh repair: retrospective single-center study including 524 patients with 3 years' median follow-up. Am J Obstet Gynecol 2012 Jan;206(1):83.e1–7. Results included an 11% reoperation rate (urinary incontinence 7%, mesh-related complications 4%, and 3% rate of recurrent prolapse). Surgery due to symptomatic mesh retraction was very rare at 0.4% (2/524), and surgery due to mesh infection was only 0.2% (1/524).

Bak, et al. did a retrospective study on 67 patients who had the Prolift procedure performed by one surgeon from May 2006 through August 2013. Bak SG, Moon JB, Hong SK, Kim KJ, Kim KA, Lee JH. A clinical study on the trocar-guided mesh repair system for pelvic organ prolapse surgery. Obstet Gynecol Sci. 2016 May;59(3):208-213. Mean age of patients was 65.4±7.2 years. Stage ≥III POP-quantification Ba was noted in 61 patients (91%). Intraoperative complications included three cases of bladder injury (4.5%). The mean follow-up period was 44.1±7.9 months. Postoperative complications occurred in seven women (10.5%): four cases of urinary symptoms (6%), two cases of infections (3%), and one case of chronic pelvic pain (1.5%). Mesh exposure did not occur (0%). Prolapse recurrence was reported in five patients (7.5%).

Da Silviera did a multicenter randomized trial comparing native vaginal tissue repair and synthetic mesh repair for genital prolapse, demonstrated an 88% cure rate for Prolift versus 81% for traditional repair. da Silveira S, et al., Multicenter, randomized trial comparing native vaginal tissue repair and synthetic mesh repair for genital prolapse surgical treatment. Int Urogynecol J 2015 Mar;26(3):335–342. Prolift patients had significantly improved quality of life. There was not a statistically significant difference in the rate of dyspareunia between native tissue repairs (6%) and Prolift (3%), nor was there a statistically significant difference

in the rate of pelvic pain between native tissue repairs (8.6%) and Prolift (2.3%). Sexual function scores per QS-F questionnaire answers were equal as well. 18 patients developed a mesh erosion and 15 were successfully treated with topical estrogen and clinical observation.

In the 2011 New England Journal of Medicine, Altman reported on a randomized trial of anterior colporrhaphy versus transvaginal mesh for pelvic organ prolapse. 389 patients were evaluated at 1 year. The success rate was significantly better in the women treated with transvaginal mesh repair (61%) as compared to those in the colporrhaphy group (35%). Altman D, et al., Anterior Colporrhaphy versus Transvaginal Mesh for Pelvic-Organ Prolapse. N Engl J Med 2011;364:1826–1836. Surgical reintervention for mesh exposure occurred in only 3% of patients in the mesh group. No significant difference between pelvic pain was noted (2 months and 12 months) between the colporrhaphy and mesh groups. Dyspareunia was reported by 2% of the women following colporrhaphy and by 7.3% after transvaginal mesh surgery; however, the rates were not statistically significantly different. Additionally, patient sexual satisfaction was 48% in the Prolift group versus only 40% in the colporrhaphy group.

In a randomized trial involving 190 patients followed for 12 months, Withagen compared Prolift with conventional vaginal repair in patients with recurrent prolapse. Withagen MI, et al., Trocar-Guided Mesh Compared With Conventional Vaginal Repair in Recurrent Prolapse: A Randomized Controlled Trial. Obstet Gynecol 2011 Feb;117(2):242–250. Follow-up rate after 12 months was 186 of 190 patients (98%). Anatomic failure in the treated compartment was observed in 38 of 84 patients (45.2%) in the conventional group and in eight of 83 patients (9.6%) in the mesh group (P<.001). Pelvic pain and dyspareunia for both groups decreased at a similar rate at 1 year compared to baseline. De novo dyspareunia occurred in 10% of the mesh group and 8% in the Prolift group. There was a 16.9% mesh exposure rate (n=14) with nine being asymptomatic. Five exposures resolved after excision.

In addition to numerous other studies that could be specifically discussed showing that Prolift can be performed safely and effectively, in 2013, the American Urogynecologic Society ("AUGS") issued a Position Statement on Restriction of Surgical Options for Pelvic Floor Disorders which noted that it is "strong opinion" that "there are subsets of women with prolapse, and in some cases those with the most advanced disease, in whom the benefits of transvaginal mesh outweigh the risks and a blanket ban on the use of these products compromises patient care." A 2011 position statement from the American Urologic Association ("AUA") similarly acknowledged that: "mesh may improve long term anatomic results of surgery as compared to non-mesh repairs for some types of prolapse. Certain patients may benefit from mesh techniques, and the use of mesh techniques should be a choice that is made after a careful discussion between surgeon and patient." These studies and professional organizations recognize that there are patients who benefit from transvaginal mesh augmentation, including Gynemesh PS and the Prolift.

KNOWN RISKS AND ALLEGED DESIGN FLAWS

All surgical techniques to treat pelvic organ prolapse, including those incorporating mesh, have advantages and disadvantages. While use of transvaginal mesh may improve long-term anatomic results, there are certain known complications that must also be considered. These complications, such as erosion, pain, urinary tract injury, and sexual dysfunction, may be due to patient anatomy, surgical technique, materials used, or a combination of those factors. Complications associated with mesh augmented repair surgeries are also commonly known to occur with non-mesh-based repairs and are not unique to use of mesh.

For example, exposure or erosion of permanent sutures or other graft materials can occur with abdominal sacrocolpopexy and other non-mesh procedures, with rates as high as 45%. Toglia MR, Fagan MJ. Suture erosion rates and long-term surgical outcomes in patients

undergoing sacrospinous ligament suspension with braided polyester suture. Am J Obstet Gynecol. 2008 May,198(5):600.e1-4; Abed H, et al.; Systematic Review Group of the Society of Gynecologic Surgeons. Incidence and management of graft erosion, wound granulation, and dyspareunia following vaginal prolapse repair with graft materials: a systematic review. Int Urogynecol J. 2011 Jul; 22(7):789-98; Yazdany T, et al. Suture complications in a teaching institution among patients undergoing uterosacral ligament suspension with permanent braided suture. Int Urogynecol J. 2010 Jul;21(7):813-8.

Mesh exposure is usually a minor complication that can be managed with use of vaginal estrogen cream, by excision in the office, or a minor outpatient procedure, and with correct technique and appropriate patient selection, this risk can be minimized. 2007 Prolift Surgeons Resource Monograph. As the literature discussed in this report indicates, as well as my own personal experience, the majority of patient outcomes are good once this complication has been identified and addressed appropriately.

It should also be noted that alternative procedures such as the abdominal sacrocolpopexy increase certain risks such as bowel obstruction, abdominal wound infection, abdominal hernia, sacral osteomyelitis, and major vessel injury. Laparoscopic and robotic procedures also have certain increased risks such as increased operative time, insufflation, steep Trendelenburg positioning, and instrument injuries.

DYSPAREUNIA and MESH CONTRACTURE

Pain with sexual intercourse is a very common complaint at baseline in women in general. Dietz and Maher noted that up to 64% of sexually active women attending a urogynecology clinic suffer from female sexual dysfunction. Dietz V, Maher C., Pelvic organ prolapse and sexual function. Int Urogynecol J. 2013 Nov;24(11):1853-7. Laumann, et al. reported a 43% rate of sexual dysfunction in the United States. Laumann EO, Paik A, Rosen

RC, Sexual dysfunction in the United States: prevalence and predictors. Jama 1999 Feb 10;281(6):537–544. Abnormal sexual function is complex, multifactorial and difficult to define. Sexual function can be affected by psychological, sociological, environmental and physical factors including vaginal atrophy, decreased libido, muscular pain or spasm and partner issues. Gynecological surgery in general, especially hysterectomy and prolapse surgery, is a well known cause of dyspareunia. These procedures can result in scar formation, vaginal tightening and shortening. There have been numerous RCTs and meta-analyses which have shown that Gynemesh PS and Prolift are not associated with an increased risk of dyspareunia compared to alternative procedures available. Dietz and Maher performed a meta-analysis of over 25 studies, including 7 randomized controlled trials, and found that there was no difference in post-operative dyspareunia, de novo dyspareunia or PISQ-12 scores. Dietz V, Maher C, Pelvic organ prolapse and sexual function. Int Urogynecol J. 2013 Nov;24(11):1853-7. The Cochrane review has reported similar findings that there was no increased rate of dyspareunia with transvaginal mesh augmentation compared to traditional prolapse repair without mesh. Maher C, Feiner B, Baessler K, Christmann-Schmid C, Haya N, Marjoribanks J. Transvaginal mesh or grafts compared with native tissue repair for vaginal prolapse. Cochrane Database of Systematic Reviews 2016; Maher C, et al., Surgical management of pelvic organ prolapse in women. Cochrane Database of Systemic Reviews 2013. Other RCTs showing no overall difference in de novo dyspareunia, de novo pelvic pain, sexual functioning by PISQ scores, change in total vaginal length and change in vaginal diameter and volume include, among others: Withagen MI, et al., Trocar-Guided Mesh Compared With Conventional Vaginal Repair in Recurrent Prolapse: A Randomized Controlled Trial. Obstet Gynecol 2011 Feb;117(2):242–250; Carey M, et al., Vaginal repair with mesh versus colporrhaphy for prolapse: a randomised controlled trial. Br J Obstet Gynecol 2009 Sep;116(10):1380–1386; Sokol AI, et al., One-year objective and

functional outcomes of a randomized clinical trial of vaginal mesh for prolapse. Am J Obstet Gynecol 2012 Jan;86:e1–e9; Altman D, et al., Anterior Colporrhaphy versus Transvaginal Mesh for Pelvic-Organ Prolapse. N Engl J Med 2011;364:1826–1836; Halaska M, et al., A multicenter, randomized, prospective, controlled study comparing sacrospinous fixation and transvaginal mesh in the treatment of posthysterectomy vaginal vault prolapse. Am J Obstet Gynecol 2012;207:301.e1–7; da Silveira S, et al., Multicenter, randomized trial comparing native vaginal tissue repair and synthetic mesh repair for genital prolapse surgical treatment. Int Urogynecol J 2015 Mar;26(3):335–342.

Mesh contracture is a potential complication from transvaginal mesh augmentation. The mesh does not actually contract but the scar tissue that may form around the mesh can result in tissue contracture. The risk of Prolift resulting in a symptomatic tissue contracture is low as per my personal experience as well as that reported in the literature. For example, in a study of 524 Prolift patients with a median follow-up of 38 months, de Landsheere et al. reported a 0.4% (2/524) rate of surgery for symptomatic mesh contraction. de Landsheere L, et al. Surgical intervention after transvaginal Prolift mesh repair: retrospective single-center study including 524 patients with 3 years' median follow-up. Am J Obstet Gynecol. 2012 Jan.; 206(1):83.e1-7. A meta-analysis of surgical complications following prolapse repair in almost 17,000 patients concluded that total complication rates were similar for traditional vaginal surgeries, sacral colpopexies, and vaginal mesh kits and did not identify mesh contraction as a common complication. Diwadkar GB, Barber MD, Feiner B, Maher C, Jelovsek JE, Complication and reoperation rates after apical vaginal prolapse surgical repair: a systematic review. Obstet Gynecol. 2009 Feb;113(2 Pt 1):367-73. Lowman, et al. reviewed 129 Prolift cases performed from 2005 to 2007. They concluded that pelvic organ prolapse repair, whether abdominal or vaginal, appears to have a relatively high rate of associated dyspareunia. Joye K. Lowman, MD,

MPH; Leticia A. Jones, MD; Patrick J. Woodman, DO; Douglass S. Hale, MD. Does the Prolift system cause dyspareunia American Journal of Obstetrics & Gynecology, Volume 199, Issue 6, 707.e1-707.e6. However, the Prolift procedure had a de novo dyspareunia rate comparable to traditional repairs.

The 2013 Cochrane review, which included almost 6,000 patients, found that no patient had mesh removed due to pain or contraction. Maher C, et al., Surgical management of pelvic organ prolapse in women. Cochrane Database of Systemic Reviews 2013. It should be noted that the 2010 Feiner and Maher article which discusses mesh contraction reported a 100% success rate in relieving or improving symptoms of mesh contraction after surgery.

INFLAMMATION, INFECTION AND DEGRADATION

All foreign materials, including sutures, allografts, xenografts and autografts cause some degree of host immune response that can result in varying degrees of tissue inflammation. Polypropylene causes less inflammation than other mesh and suture materials. As per the extensive general surgery literature on hernia management and later the pelvic organ prolapse experience (as previously discussed), polypropylene is now standard of care for mesh augmented vaginal hernia repair, abdominal hernia repair and the treatment of stress urinary incontinence. The studies cited above further demonstrate that there is no clinical basis for a claim that polypropylene causes an excessive inflammatory reaction which results in a high percentage of negative clinical outcomes.

In addition, numerous meta-analyses and systematic reviews show that infection of the mesh is exceedingly rare. For example, Dyrkorn, et al. reported an infection rate of 0.7%. I have personally implanted mesh for more than 15 years and I have only observed mesh infection on one instance that I am aware of, which involved a transobturator sling implanted by another

physician. Similarly, any allegations that there are design flaws in polypropylene mesh because it allows bacteria to adhere to the mesh during implantation causing clinical infection are not supported by the substantial amount of medical literature which demonstrates the safety and efficacy of polypropylene mesh used for both prolapse repairs and to treat stress urinary incontinence.

Polypropylene in the form of suture and mesh has been used for decades. I am not aware of any evidence both personally or in the literature that suggests that this substance degrades in the human body, and certainly nothing suggesting that any such degradation is responsible for any clinically significant sequelae (which again is evidenced by the numerous studies cited in this report). The sub-specialty societies AUGS and SUFU have also specifically addressed whether polypropylene mesh degrades over time and whether any such degradation leads to adverse clinical outcomes. AUGS-SUFU dismissed these concerns pointing to extensive peer-reviewed literature related to polypropylene mesh:

> Polypropylene is a stable and well-accepted biomaterial with a history of over five decades of use in mesh implants. In recent years, concerns regarding implanted polypropylene degradation have been raised as a result of very high-magnification images that show portions of some explanted synthetic meshes with "cracked" surfaces. These surface changes were further hypothesized to lead to adverse clinical outcomes, though this is not supported by the extensive peer-reviewed literature related to polypropylene mesh repairs. Prospective studies have followed patients with implanted mid-urethral slings for 17 years and show excellent durability and safety of the procedure.

As noted in the above-referenced AUGS-SUFU statement, concerns regarding degradation are based largely on reports that have detected "cracked surfaces" along portions of explanted synthetic mesh using very high scanning electron microscope magnification. These reports have hypothesized that the microscopic observations could result in adverse clinical outcomes, but that theory is inconsistent with the extensive peer-reviewed literature related to polypropylene mesh repair. My experience and analysis of the data, including the studies cited

in my report, supports my opinion that Ethicon's polypropylene mesh does not degrade in vivo, or if it does, that such degradation does not have any clinically significant effect.

CYTOTOXICITY AND CANCER

I am not aware of any evidence that polypropylene, when used as designed for its intended purpose as a mesh implant or as a suture material, has any clinically significant cytotoxic or cancer-causing effect. Polypropylene was developed in the 1950s. Aside from other daily forms of human contact, it has been used in countless millions of surgical procedures over the past 60 years. Common sense would dictate that based on the amount polypropylene material used in a surgical setting since its development in the 1950s, if there was a clinically significant problem, it would be a worldwide catastrophe at this point.

Moalli, et al. addressed this issue. Pamela Moalli, Bryan Brown, Maureen T. F. Reitman, Charles W. Nager. Polypropylene mesh: evidence for lack of carcinogenicity. International Urogynecology Journal May 2014, Volume 25, Issue 5, pp 573–576. They concluded that polypropylene, which has been used extensively in humans for over five decades, is not associated with carcinogenesis. AUGS-SUFU also addressed this issue. "There is no compelling evidence supporting human malignant transformation related to polypropylene despite the millions of individuals implanted with various forms of this material span well over a half century world-wide." AUGS-SUFU FAQs by Patients on Mid-urethral Slings for SUI March 2014. Type 1 macroporous, monofilament polypropylene has been found to be the most biocompatible biomaterial for use in the pelvic floor. Ford AA, et al., Mid-urethral sling operations for stress urinary incontinence in women. Cochrane Database of Systemic Reviews 2015.

Further data from research on midurethral polypropylene slings also indicates lack of cancer risk. King et al., 2014 reported on 2,361 patients who underwent synthetic sling

placement, and found one case each of bladder and vaginal cancer for an incidence of 0.08%, with mean follow-up of 42 months. King AB, et al. Is there an association between polypropylene midurethral slings and malignancy? Urology. 2014 Oct;84(4):789-92; King AB, Goldman HB. Current controversies regarding oncologic risk associated with polypropylene midurethral slings. Curr Urol Rep. 2014 Nov;15(11):453. Linder discovered only two cases amongst 2,474 who underwent polypropylene mid-urethral sling placement (0.08%) with a mean follow-up of 61.5 months. Linder BJ, et al., Evaluation of the local carcinogenic potential of mesh used in the treatment of female stress urinary incontinence. Int Urogynecol J 2016 DOI:10.1007/s00192-016-2961-4. Linder further found that no local cancers were detected among the 302 patients (12% of the cohort) with more than 10 years' follow-up. There is no reliable data demonstrating an association between mesh placement with subsequent cancer formation.

COMMUNICATION OF RISK INFORMATION AND PROFESSIONAL EDUCATION

It is my opinion based on my knowledge and experience as a female pelvic reconstruction surgeon, as well as the medical literature, my training of other doctors, and my attendance at professional meetings, that Prolift IFU and professional education materials adequately described the risks specific to the Prolift. It is notable that the IFU specifically states that "users should be familiar with surgical procedures and techniques involving pelvic floor repair and synthetic meshes" before using the Prolift device. This is significant because the IFU is written for surgeons who learn how to perform any surgery in residency, fellowship, and through proctorship. It is expected that these surgeons would be experienced and knowledgeable regarding these procedures as part of meeting their standard of care. ABOG and ABU Guidelines for Learning in Female Pelvic Medicine & Reconstructive Surgery; AUGS Resident Learning Objectives. Pelvic floor surgeons do not learn how to perform surgical procedures or

the risks associated with performing surgical procedures by reading an IFU. Rather, we learn these things from training, dialogue with colleagues, attendance at professional meetings, and through review of published medical literature. Surgeons are responsible for understanding the inherent risks of the surgical procedures they perform, and surgeons are also responsible for continuing to reviewing medical literature to stay up-to-date on data related to the procedures they perform.

As I have already noted above, all pelvic floor surgical procedures have certain commonly known risks. And the risks associated with the Prolift procedure are almost all common to any pelvic floor surgery regardless whether mesh is utilized. Weber AM, Walters MD, Anterior vaginal prolapse: review of anatomy and techniques of surgical repair. Obstet Gynecol. 1997;89:311–318. These risks have been discussed in medical literature discussing pelvic floor surgeries for decades. It is commonly known that any surgery for pelvic organ prolapse can potentially cause complications such as pelvic pain, nerve/vessel injury, scarring, wound complications, bleeding, damage to surrounding organs, voiding problems/retention, dyspareunia, de novo or worsened incontinence, and the need for re-operation due to complications. Surgeons also commonly know that these complications can be mild, moderate, or severe, and temporary or long-term.

The Prolift IFU warned of several risks including infection potentiation, inflammation, adhesion formation, fistula formation, erosion, extrusion and scarring that results in implant contraction. All pelvic floor surgeons know this based on their training and basic knowledge that these complications may cause sequela such as pain and dyspareunia, or the need to re-operate.

While I am not a regulatory expert, I have reviewed and considered 21 C.F.R. 801.109(c), which states that risk information for devices used by licensed professionals may be omitted from product labeling if "the article is a device for which directions, hazards, warnings, and other

information are commonly known to practitioners licensed by law to use the device." This regulation further supports my opinions because identifying not only complications, but also implications of each complication, is not necessary for pelvic floor surgeons and would require a medical treatise to accompany every product.

With respect to physician training and professional education, the manufacturer is not responsible for training surgeons how to perform surgeries, but it is my opinion that it is a very good idea for Ethicon to offer professional education courses where surgeons could get exposure to experts in this area of medicine. Having taught courses for Ethicon involving the Prolift, I know that each course involved a thorough discussion of the data regarding the safety and efficacy of the product. Participants were provided not only the IFU, but also training videos and other written materials. The 2007 Prolift Surgeon's Monograph is an example of one such document that was distributed to physicians, and it is one of the most comprehensive education materials I have reviewed. The training that Ethicon offers is intended to supplement the surgeon's training from residency, fellowship and proctorships, and it should not be viewed as a surgeon's primary source of surgical expertise. Each individual surgeon must determine whether he/she has the surgical skill, training, and knowledge to offer a particular product/procedure to their patients. I have participated in trainings offered by numerous other manufacturers and it is my opinion that the trainings and materials offered by Ethicon are tremendous.

FEES

I am currently being paid $500.00 per hour for my time to review medical records and draft written reports; $600.00 per hour for in-town depositions ($6,000.00 per day for out-of-town depositions); and $5,000.00 per day for in-town trial testimony ($6,000 per day for out-of-town trial testimony). I have not testified as a retained expert witness in either a trial or deposition in the last 4 years.

The opinions set forth in my report are based on the information that is currently available to me. I reserve the right to modify or amend these opinions if new information becomes available.

Steven Goldwasser, M.D.
February 15, 2017